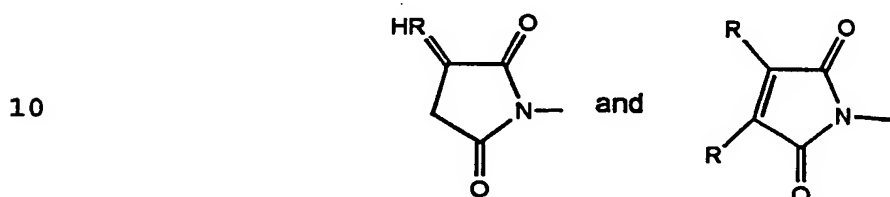


CLAIMS

1. A polymerisation process in which ethylenically unsaturated monomers including a zwitterionic monomer of the general formula I



5 in which Y is an ethylenically unsaturated group selected from $\text{H}_2\text{C}=\text{CR}-\text{CO}-\text{A}-$, $\text{H}_2\text{C}=\text{CR}-\text{C}_6\text{H}_4-\text{A}^1-$, $\text{H}_2\text{C}=\text{CR}-\text{CH}_2\text{A}^2$, $\text{R}^2\text{O}-\text{CO}-\text{CR}=\text{CR}-\text{CO}-\text{O}$, $\text{RCH}=\text{CH}-\text{CO}-\text{O}$, $\text{RCH}=\text{C}(\text{COOR}^2)\text{CH}_2-\text{CO}-\text{O}$,



A is $-\text{O}-$ or NR^1 ;

15 A^1 is selected from a bond, $(\text{CH}_2)_n\text{A}^2$ and $(\text{CH}_2)_n\text{SO}_3^-$ in which n is 1 to 12;

A^2 is selected from a bond, $-\text{O}-$, $\text{O}-\text{CO}-$, $\text{CO}-\text{O}$, $\text{CO}-\text{NR}^1-$, $-\text{NR}^1-\text{CO}$, $\text{O}-\text{CO}-\text{NR}^1-$, $\text{NR}^1-\text{CO}-\text{O}-$;

R is hydrogen or C_{1-4} alkyl;

R^1 is hydrogen, C_{1-4} alkyl or BX ;

20 R^2 is hydrogen or C_{1-4} alkyl;

B is a bond, or a straight branched alkanediyl, alkylene oxaalkylene, or alkylene (oligooxaalkylene) group, optionally containing one or more fluorine substituents;

X is a zwitterionic group

25 are polymerised by a living radical polymerisation process in the presence of an initiator, and a catalyst;

in which the initiator is a compound of general formula V



30 where:

Y is selected from the group consisting of Cl, Br, I, OR^{10} , SR^{14} , SeR^{14} , $\text{OP}(=\text{O})\text{R}^{14}$, $\text{OP}(=\text{O})(\text{OR}^{14})_2$, $\text{O}-\text{N}(\text{R}^{14})_2$ and $\text{S}-\text{C}(=\text{S})\text{N}(\text{R}^{14})_2$, where R^{10} is

alkyl of from 1 to 20 carbon atoms in which each of the hydrogen atoms may be independently replaced by halide, R^{14} is aryl or a straight or branched C_1 - C_{20} alkyl group, and where an $N(R^{14})_2$ group is present, the two R^{14} groups may be joined to form a 5- or 6-membered heterocyclic ring;

5 R^{11} and R^{12} are each independently selected from the group consisting of H, halogen, C_1 - C_{20} alkyl, C_3 - C_8 cycloalkyl, $C(=O)R^{15}$, $C(=O)NR^{16}R^{17}$, $COCl$, OH , CN , C_2 - C_{20} alkenyl, oxiranyl, glycidyl, aryl, heterocyclyl, aralkyl and aralkenyl, in any of which the alkyl, alkenyl or aryl, heterocyclyl or cycloalkyl groups there may be from 1 to 3 substituents
10 selected from the group consisting of hydrogen, hydroxy C_1 - C_4 alkoxy, acyloxy, aryl, heterocyclyl, $C(=O)R^{15}$, $C(=O)NR^{16}R^{17}$, $-CR^{12}R^{13}Y$, $CR^{11}R^{12}Y$, oxiranyl and glycidyl;

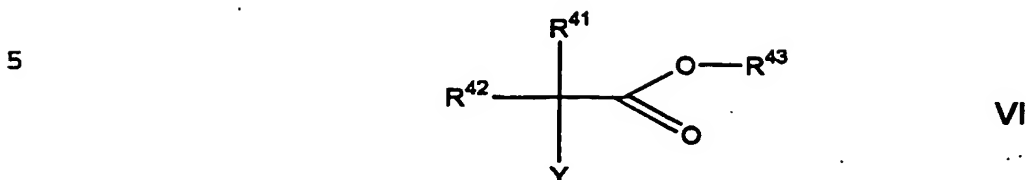
where R^{15} is alkyl of from 1 to 20 carbon atoms, alkoxy of from 1 to 20 carbon atoms, oligo(alkoxy) in which each alkoxy group has 1 to 3 carbon
15 atoms, aryloxy or heterocyclyloxy any of which groups may have substituents selected from optionally substituted alkoxy, oligoalkoxy, amino (including mono- and di-alkyl amino and trialkyl ammonium, which alkyl groups, in turn may have substituents selected from acyl, acyloxy, alkoxy, alkoxycarbonyl, alkenoxycarbonyl, aryl and hydroxy), and hydroxyl groups;

20 R^{16} and R^{17} are independently H or alkyl of from 1 to 20 carbon atoms which alkyl groups, in turn may have substituents selected from alkoxy, acyl, acyloxy, alkoxycarbonyl, alkenoxycarbonyl, aryl and hydroxy, or R^{16} and R^{17} may be joined together to form an alkanediyl group of from 2 to 5 carbon atoms, thus forming a 3- to 6-membered ring; and

25 R^{13} is selected from the group consisting of biologically active group-substituted alkyl, cycloalkyl, $-COR^{15}$, $-CONR^{16}R^{17}$, alkenyl, aryl, heterocyclyl, aralkyl and aralkenyl groups, in any of which the alkyl, alkenyl, aryl, heterocyclyl or cycloalkyl groups may have from 1 to 3 substituents selected from the group consisting of hydrogen, hydroxy, C_1 - C_4 alkoxy, acyloxy, aryl,
30 heterocyclyl, $C(=O)R^{15}$, $C(=O)NR^{16}R^{17}$, $-CR^{12}R^{13}Y$, $CR^{11}R^{12}Y$, oxiranyl and glycidyl where R^{15} , R^{16} and R^{17} are groups as defined above for R^{11} and R^{12} with the biologically active group substituted on an alkyl cycloalkyl, alkenyl,

aryl or heterocyclyl group.

2. A process according to claim 2 in which the initiator is a compound of general formula VI



10 where R^{41} and R^{42} are independently selected from hydrogen, straight, branched and cyclic alkyl, aryl, aralkyl, hydroxy-alkyl and acyloxyalkyl.

R^{43} is a biologically active moiety; and

Y as defined in claim 1 and is preferably a halogen atom.

3. A process according to claim 3 in which R^{41} and R^{42} are not both hydrogen, preferably in which either

- 15 a) R^{41} and R^{42} are each methyl; or
b) R^{41} is hydrogen and R^{42} is methyl.

4. A process according to claim 1 in which the biologically active moiety is a steroid moiety, for instance a cholesterol moiety.

20 5. A process according to claims 2 or claim 3 in which R^{43} is derived from a pharmaceutically or diagnostically active alcohol $R^{43}OH$.

6. A process according to claim 5 in which $R^{43}OH$ is a carbohydrate, for instance a saccharide.

25 7. A process according to claim 3 or claim 4 in which R^{43} is $R^{44}AL$ -derived from $R^{44}ALOH$ in which R^{44} is derived from a pharmacologically or diagnostically active compound $R^{44}AH$ where A is a divalent moiety selected from the group consisting of O, NR^{35} (R^{35} is H or lower alkyl), COO and $CONR^{35}$, and L is a divalent linker.

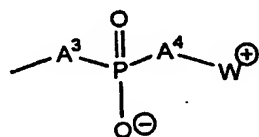
8. A process according to claim 7 in which L is an oligo-peptide-based linker.

30 9. A process according to any preceding claim in which the product polymer has a molecular weight in the range 1000 to 100,000, preferably 2,000 to 50,000, preferably less than 10,000.

10. A process according to any preceding claim in which the product polymer has a polydispersity less than 1.5, preferably less than 1.2.

11. A process according to any preceding claim in which X is an ammonium, phosphonium, or sulphonium phosphate or phosphonate ester
5 zwitterionic group.

12. A process according to claim 12 in which X is a group of the general formula II



II

10

in which the moieties A^3 and A^4 , which are the same or different, are -O-, -S-, -NH- or a valence bond, preferably -O-, and W^{\oplus} is a group comprising an ammonium, phosphonium or sulphonium cationic group and a
15 group linking the anionic and cationic moieties which is preferably a C_{1-12} -alkanediyl group,

preferably in which W^{\oplus} is a group of formula
- W^1 - $\text{N}^{\oplus}\text{R}^3_3$, - W^1 - $\text{P}^{\oplus}\text{R}^4_3$, - W^1 - $\text{S}^{\oplus}\text{R}^4_2$ or - W^1 -Het $^{\oplus}$ in which:

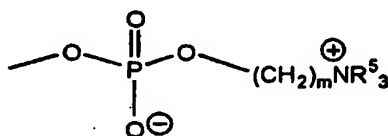
W^1 is alkanediyl of 1 or more, preferably 2-6 carbon atoms optionally
20 containing one or more ethylenically unsaturated double or triple bonds, disubstituted-aryl (arylene), alkylene arylene, arylene alkylene, or alkylene aryl alkylene, cycloalkanediyl, alkylene cycloalkyl, cycloalkyl alkylene or alkylene cycloalkyl alkylene, which group W^1 optionally contains one or more fluorine substituents and/or one or more functional groups; and

25 either the groups R^3 are the same or different and each is hydrogen or alkyl of 1 to 4 carbon atoms, preferably methyl, or aryl, such as phenyl, or two of the groups R^3 together with the nitrogen atom to which they are attached form an aliphatic heterocyclic ring containing from 5 to 7 atoms, or the three groups R^3 together with the nitrogen atom to which they are
30 attached form a fused ring structure containing from 5 to 7 atoms in each ring, and optionally one or more of the groups R^3 is substituted by a hydrophilic functional group; and

the groups R^4 are the same or different and each is R^3 or a group OR^3 , where R^3 is as defined above; or

Het is an aromatic nitrogen-, phosphorus- or sulphur-, preferably nitrogen-, containing ring, for example pyridine.

- 5 13. A process according to claim 12 in which X is a group of general formula III



III

10

where the groups R^5 are the same or different and each is hydrogen or C_{1-4} alkyl, and m is from 1 to 4, in which preferably the groups R^5 are the same preferably methyl.

14. A process according to any preceding claim in which Y is
15 $H_2C=CR-CO-A-$ in which R is hydrogen or methyl and A is O.

15. A polymerisation process according to any preceding claim in which B is a straight chain C_{2-8} -alkanediyl.

16. A polymerisation process according to claim 1 in which the
20 zwitterionic monomer is 2-methacryloyloxyethyl-2'-trimethylammonium ethyl phosphate inner salt.

17. A polymerisation process according to any preceding claim in which the polymerisation mixture contains a non-polymerisable solvent, preferably in an amount, in the range of 10 to 500% by weight based on the weight of ethylenically unsaturated monomer.

- 25 18. A polymerisation process according to any preceding claim in which the ethylenically unsaturated monomer includes at least one comonomer, preferably selected from anionic, cationic and non-ionic monomers, more preferably comprising a non-ionic monomer.

- 30 19. A polymerisation process according to any preceding claim in which the catalyst comprises a transition metal compound and a ligand, in which the transition metal compound is capable of participating in a redox cycle with the initiator and dormant polymer chain, and the ligand is either

any N-, O-, P- or S- containing compound which can coordinate with the transition metal atom in a σ -bond, or any carbon-containing compound which can coordinate with the transition metal in a π -bond, such that direct bonds between the transition metal and growing polymer radicals are not formed.

5 20. A polymerisation process according to claim 20 in which the transition metal compound $M_t^{n+}X'_n$, where:

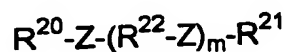
M_t^{n+} may be selected from the group consisting of Cu^{1+} , Cu^{2+} , Fe^{2+} , Fe^{3+} , Ru^{2+} , Ru^{3+} , Cr^{2+} , Cr^{3+} , Mo^{2+} , Mo^{3+} , W^{2+} , W^{3+} , Mn^{2+} , Mn^{3+} , Mn^{4+} , Rh^{3+} , Rh^{4+} , Re^{2+} , Re^{3+} , Co^{+} , Co^{2+} , Co^{3+} , V^{2+} , V^{3+} , Zn^{+} , Zn^{2+} , Ni^{2+} , Ni^{3+} , Au^{+} , Au^{2+} , Ag^{+} and Ag^{2+} ;

10 X' is selected from the group consisting of halogen, C_{12} - C_6 -alkoxy, $(SO_4)_{1/2}$, $(PO_4)_{1/3}$, $(R^{18}PO_4)^{1/2}$, $(R^{18}_2PO_4)$, triflate, hexafluorophosphate, methanesulphonate, arylsulphonate, CN and $R^{19}CO_2$, where R^{18} is aryl or a straight or branched C_{1-20} alkyl and R^{19} is H or a straight or branched C_1 - C_6 alkyl group which may be substituted from 1 to 5 times with a halogen; and
15 n is the formal charge on the metal ($0 \leq n \leq 7$).

21. A polymerisation process according to claim 20 in which the metal compound is $CuHal$ or $RuHal_2$ where Hal is chlorine or bromine.

22. A polymerisation process according to any of claims 19 to 21
20 wherein said ligand is selected from the group consisting of:

a) compounds of the formulas:



25

where:

R^{20} and R^{21} are independently selected from the group consisting of H, C_1 - C_{20} alkyl, aryl, heterocyclyl and C_1 - C_6 alkoxy, C_1 - C_4 dialkylamino, $C(=O)R^{22}$, $C(=O)R^{23}R^{24}$ and $A^7C(=O)R^{25}$, where A^7 may be NR^{26} or O; R^{22} is
30 alkyl of from 1 to 20 carbon atoms, aryloxy or heterocyclyloxy; R^{23} and R^{24} are independently H or alkyl of from 1 to 20 carbon atoms or R^{23} and R^{24} may be joined together to form an alkanediyl group of from 2 to 5 carbon

atoms, thus forming a 3- to 6-membered ring; R^{25} is H, straight or branched C_1 - C_{20} alkyl or aryl and R^{26} is hydrogen, straight or branched; C_1 - C_{20} -alkyl or aryl; or R^{20} and R^{21} may be joined to form together with Z, a saturated or unsaturated ring;

5 Z is O, S, NR^{27} or PR^{27} , where R^{27} is selected from the same group as R^{20} and R^{21} , and where Z is PR^{27} , R^{27} can also C_1 - C_{20} alkoxy or Z may be a bond CH_2 or a fused ring, where one or both of R^{20} and R^{21} is heterocyclyl, each R^{22} is independently a divalent group selected from the group consisting of C_1 - C_8 cycloalkanediyl, C_1 - C_8 cycloalkanediyl, arenediyl and
10 heterocyclylene where the covalent bonds to each Z are at vicinal positions or R^{22} may be joined to one or both of R^{20} and R^{21} to formulate a heterocyclic ring system; and

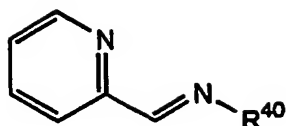
m is from 1 to 6;

b) CO;

15 c) porphyrins and porphycenes, which may be substituted with from 1 to 6 halogen atoms, C_1 - C_6 alkyl groups, C_1 - C_6 -alkoxy groups, C_1 - C_6 alkoxycarbonyl, aryl groups, heterocyclyl groups, and C_1 - C_6 alkyl groups further substituted with from 1 to 3 halogens;
20 d) compounds of the formula $R^{23}R^{24}C(C(=O)R^{25})_2$, where R^{25} is C_1 - C_{20} alkyl, C_1 - C_{20} alkoxy, aryloxy or heterocycliloxy; and each of R^{23} and R^{24} is independently selected from the group consisting of H, halogen, C_1 - C_{20} alkyl, aryl and heterocyclyl, and R^{23} and R^{24} may be joined to form a C_1 - C_8 cycloalkyl ring or a hydrogenated aromatic or heterocyclic ring, of which the ring atoms may be further substituted with 1 to 5 C_1 - C_6 alkyl groups, C_1 - C_6 alkoxy groups,
25 halogen atoms, aryl groups, or combinations thereof; and

e) arenes and cyclopentadienyl ligands, where said cyclopentadienyl ligand may be substituted with from one to five methyl groups, or may be linked through an ethylene or propylene chain to a second cyclopentadienyl ligand.

30 23. A polymerisation process according to claim 22 in which the ligand is bipyridine, triphenylphosphine, 1,1,4,7,10,10-hexamethyl-triethylene tetramine, or a compound of the general formula VII

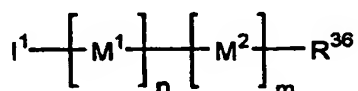


VII

5 where R^{40} is an alkyl or substituted alkyl group, in which the substituent is selected from amino, including alkylamino and acylamino, alkoxy, hydroxy, acyl, acyloxy, alkoxycarbonyl, heterocyclyl, ionic, and halogen substituents.

24. A compound comprising a conjugate of a biologically active moiety and a polymeric group having a general formula:

10

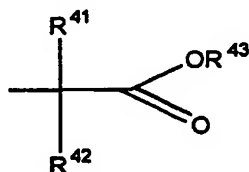


VIII

in which M^1 is the divalent group formed when the compound of the general formula I as defined in claim 1 is polymerised, M^2 is the divalent group
15 formed when a comonomer as defined in claim 19 is polymerised, and I^1 is the residue of the initiator defined in claim 1 which comprises said biologically active moiety, and R^{36} is a monofunctional group or atom which terminates the polymeric group M^1 , n is at least 2 and m is at least 0.

25. A compound according to claim 24 in which I^1 is $-CR^{11}R^{12}R^{13}$ in
20 which R^{11} to R^{13} are as defined in claim 2.

26. A compound according to claim 24 in which I^1 is a group



25

in which R^{41} , R^{42} and R^{43} are as defined in any of claims 2 to 8.

27. A compound according to any of claims 24 to 26 in which the compound has a molecular weight in the range 1000 to 100,000, preferably 20,000 to 50,000.

30 28. A compound according to any of claims 24 to 27 which has a polydispersity less than 1.5, preferably less than 1.2.

29. A compound according to any of claims 24 to 38 in which M^1 is

the divalent group formed when a compound of the general formula I as defined in any of claims 12 to 17 is polymerised.

30. A compound according to claim 24 in which groups M^1 and M^2 are randomly arranged.

5 31. A compound according to claim 24 in which the polymeric group is a block polymeric group, in which one block comprises residues M^1 and another block comprises residues M^2 , and in which either the M^1 -containing block, or the M^2 containing block is attached to I^1 .

10 32. A compound according to any of claims 24 to 31 which is soluble in water.